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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/485,598	02/14/2000	BERNARD CHARLES SHERMAN	2051-36	6120

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EXAMINER	
PULLIAM, AMY E	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 05/31/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/485,598	Applicant(s) SHERMAN, BERNARD CHARLES	
	Examiner Amy E Pulliam	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/28/02* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Receipt is acknowledged of the Extension of Time and Amendment C, both received by the Office on March 28, 2002.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-20 are rejected under 35 U.S.C. 103(q) as being unpatentable by US Patent 5,776,495 to Duclos *et al.*. in view of US Patent 4,820,833 to Crisp *et al.*. Dulcos *et al.* disclose a process for the production of a solid dispersion of at least one therapeutic agent in a carrier, comprising dissolving at least one therapeutic agent in an organic solvent containing a very hydrophilic polymer and evaporating the solvent to dryness to form a co-precipitate of therapeutic agent and hydrophilic polymer. Duclos *et al.* also teach the products which result from the co-precipitate and their therapeutic methods of use. (abstract). Duclos *et al.* further teach a wide range of active ingredients which can be used in the formulation, including cefuroxime (c 5, l 10). Duclos *et al.* teach that examples of the organic solvent include ethanol and acetone, among others (c 3, l 10-20). Duclos *et al.* teach the co-precipitate with a hydrophilic polymer, in general, but they specifically teach the use of polyvinylpyrrolidone (c 2, l 30-32).

Duclos *et al.* does not specifically teach the use of sorbitol as the water soluble excipient. However, it is the position of the examiner that one of ordinary skill in the pharmaceutical art knows that sorbitol, mannitol, hydroxypropylmethyl cellulose, and polyvinylpyrrolidone are all very well known, and often interchangeable excipients. Therefore, one of ordinary skill in the art would have motivation to use any of these well known, and often interchangeable excipients in the formulation disclosed by Duclos *et al.*. Additionally, Duclos *et al.* stresses that the important function of the excipient is that it be hydrophilic, so any of these well known additives would apply. One of ordinary skill in the art would expect the same result, regardless of what well known hydrophilic pharmaceutical excipient is used.

Additionally, Duclos *et al.* does not go into details regarding each disclosed active agent, such as teaching specific forms of each disclosed active, or disclosing specific percentages of each disclosed active. However, it is the position of the examiner that the a discussion of the appropriate forms and percentages for each active disclosed by Duclos *et al.* would be unnecessary. It is further the position of the examiner that the specific percentage used is a limitation which would be routinely determined by one of ordinary skill in the art, through minimal experimentations, as being suitable, absent a showing of some unusual or unexpected results. The results must be those that accrue form the specific limitations.

When a skilled practitioner looks to make and use the invention of Duclose, using cefuroxime, they would look to the teachings of Crisp *et al.*. Crisp *et al.* discloses a pharmaceutical composition comprising a precipitated form of cefuroxime axetil. Crisp *et al.* discusses that this particular form of cefuroxime is beneficial because it is capable of being absorbed from the GI tract following oral administration (c 1, l 30-36). Additionally, Crisp *et al.*

teach a method of precipitating by dissolving the active in an organic solvent, and spray drying to evaporate off the solvent. One of ordinary skill in the art would look to the broad teachings of Duclos *et al.*, and apply the specific teachings of Crisp *et al.*, such as the use of the specific form cefuroxime axetil, as well as the use of spray drying to evaporate off the solvent and cause formation of the precipitate (or co-precipitate). Furthermore, Crisp *et al.* detail pharmaceutical formulations using the precipitate formed, and disclose acceptable excipients such as sodium starch glycolate (c 11, l 66).

It is the position of the examiner that Duclos *et al.* disclose applicant's generic inventive concept, which is forming a co-precipitate from a therapeutic agent (such as cefuroxime) and a water soluble excipient. It is further the position of the examiner that a skilled practitioner would look to the appropriate art, such as Crisp *et al.*, to discover more specifics concerning the specific active, cefuroxime. One of ordinary skill in the art would certainly be motivated to combine the teachings of these two references, in order to form a successful co=-precipitate of cefuroxime and a hydrophilic excipient. Therefore, this invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Applicant's arguments have been fully considered but are not found to be persuasive. Applicant's argue that Duclos includes an extensive list of actives, and further that there is no way Duclos intended or perfected an understanding of how the various actives might be incorporated in a co-precipitate formulation. Applicant further argues that Duclos gives no guidance for the use of cefuroxime, other than the listing in the list of actives. The examiner does not agree that no guidance has been given, as Duclos does teach the process of making a

co-precipitate, and also teaches that each of those actives can be used in the co-precipitate. However, the examiner has acknowledged that Duclos does not go into great detail regarding the specifics of each and every active listed in his specification. Instead, one of ordinary skill in the art would be motivated to look to related art. This is the purpose of the secondary reference, Crisp. Crisp details a pharmaceutical composition comprising cefuroxime. Furthermore, Crisp teaches that the ester form, specifically cefuroxime axetil is more successful in oral pharmaceutical dosage forms. Additionally, Crisp is relied upon for the teaching that with this particular drug, spray drying is successful to create the final precipitate. It remains the position of the examiner that one of ordinary skill in the art who is looking to practice the teachings of Duclos, and create a co-precipitate out of cefuroxime, would look to the teachings of Crisp for guidance.

Applicant also argues that Crisp is different from the instant claims because Crisp requires cefuroxime axetil in highly pure substantially amorphous form. Applicant argues that this is mutually exclusive from the instant claims, as well as the teachings of Duclos, which both require a co-precipitate. The examiner respectfully disagrees. Stedman's Medical Dictionary (attached) defines amorphous as not crystallized. The same dictionary (also attached) defines precipitate as a solid separated out from a solution or suspension. These two terms are not mutually exclusive, as claimed by applicant. No where in the Crisp reference does it prohibit precipitation. Instead the Crisp reference simply prohibits any crystalline material from being present. In fact, the Crisp reference discusses eliminating the solvent from the active and excipients in order to create a solid. In other words, the Crisp reference actually teaches precipitation.

Lastly, applicant has amended the claims to recite a specific dissolution time. However, the dissolution time claimed is very broad, stating anything greater than 10 minutes. Absent evidence to the contrary, it is the position of the examiner that the teachings of Duclos in view of Crisp would render the same results. It is recommended that applicant submit comparative data showing otherwise.

For the above reasons, this rejection is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E Pulliam whose telephone number is 703-308-4710. The examiner can normally be reached on Mon-Thurs 7:30-5:00, Alternate Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

aep
May 28, 2002

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600